REMARKS

Claims 1-8 have been cancelled and claims 9-15 added. The specification also has been amended merely to add section headings where applicable and an Abstract is provided. No new matter is added by virtue of these amendments. Support for the amendments can be found throughout the specification and in the original claims.

The following informalities have been attended to in the within Amendment. The specification has been amended to more properly conform with the 37 CFR 1.77(b). An Abstract also is provided on an attached sheet hereto.

Claims 4-8 were objected to under 37 CFR 1.75(c) for improper multiple dependencies. The subject matter of the noted claims has been rewritten in new claims 12-15 to properly conform with 37 CFR 1.75(c). Withdrawal of the objection is requested.

Claims 1-3 are rejected under 35 USC 112, 2nd paragraph. Applicants have rewritten the subject matter of original claims 1-3 in new claims 9-11 in order to further define and clarify the features of the invention. In particular, the phrase "over several days" formerly recited in claims 1 and 2, has been further defined as --over a period of up to 7 days-- . (See support therefore in the specification at page 7, lines 29-30.) Withdrawal of the rejection is therefore requested.

Claims 1-3 are rejected under 35 USC 103(a) over WO 98/03067 in view of US 5,730,999.

The rejection is traversed. Even if combined, the cited references do not teach or suggest the methods of the present invention in a manner sufficient to sustain the rejection.

For instance, WO 98/03067 ('067) does not disclose the transdermal use of tolterodine in a sufficient manner to sustain the rejection. Nor does that reference provide any technical teaching on how to carry out the transdermal application or of any specific embodiment.

Additionally, the '067 reference does not disclose a transdermal therapeutic system containing a self-adhesive, layered matrix composition in accordance with the present invention.

In contrast to the '067 reference, the present invention addresses the problem of developing a simple transdermal therapeutic system that is well-tolerated by the skin, is physically and chemically stable over longer storage and application periods, has good bonding properties and good active substance release.

The present invention is novel and non-obvious in view of the '067 reference. Indeed, in view of the limited teaching of that reference, a person skilled in the art would still have to choose between different transdermal forms, between different transdermal therapeutic systems (reservoir systems, self-adhesive systems) and different self-adhesive adhesive polymers in order to solve the problem addressed by the present invention. Applicants discovered the solution to that problem as per the present application. The problem addressed by the present application and the features of the invention were not taught or suggested by the '067 reference.

US 5,730,999 ('999) is similarly deficient and does not remedy the deficiencies of the '067 reference.

As an initial matter, before discussing the '999 patent and the nonobviousness of the present claims over the '999 patent, Applicants wish to point out an error in the '999 patent. In particular, the '999 patent states at column, 4, lines 5 and 6 that poly(meth)acrylates with functional groups include:

> Copolymer with approximately 10 wt.% quaternary ammonium groups: ®Eudragit RS 100.

At column 4, lines 31-33, the '99 patent states that a polymer without or with only insignificant amounts of functional groups includes:

> Copolymers of ethyl acrylate and methyl methacrylate with ca. 5 % trimethylammonioethyl methacrylate chloride.

Applicants respectfully submit that this is incorrect. The copolymer containing 10 wt% quaternary groups is EUDRAGIT® RL100, whereas the copolymer containing 5 % trimethylammonioethyl methacrylate chloride is EUDRAGIT RS 100. Applicants attach hereto Exhibit A, which includes a copy of a 2002 publication providing support that the '999 patent specification is in error. See, also, Assmus et al. U.S. Patent No. 6,063,399 (copy attached), which correctly defines EUDRAGIT® RL 100 and RS 100 at column 3, lines 49-59, stating:

> A (methyl)acrylate [sic] copolymer, corresponding to component (a1), with quaternary amino groups can be synthesized, for example, from 60 wt % methyl methacrylate, 30 wt. % ethyl acrylate, and 10 wt. % 2-trimethylammoniumethyl methacrylate chloride (EUDRAGIT® RL100).
>
> Another preferred (meth)acrylate copolymer corresponding to component (a1) with a quaternary amino group can be synthesized, for example, from 65 wt.% methyl methacrylate, 30 wt. % ethyl acrylate, and 5 wt. % 2-trimethylammoniumethyl methacrylate chloride (EUDRAGIT® RS 100).

Accordingly, the TTS of the present invention, and its method of manufacture, as illustrated in the Examples of the present application, contains EUDRAGIT® RS 100, or an equivalent thereof, as the sole (meth)acrylate copolymer. The present claims exclude (meth)-acrylate copolymers other than EUDRAGIT® RS 100 and its equivalents, i.e., an ethyl acrylate/methyl methacrylate copolymer containing about 5 % trimethylammonium ethyl methacrylate chloride is the sole (meth)acrylate copolymer in the matrix composition.

The '999 patent is directed to a therapeutic system that (a) necessarily contains (i) at least one (meth)acrylate polymer containing functional groups (e.g., EUDRAGIT® RL-100) and (ii) at least one (meth)-acrylic polymer that contains no or an insignificant amount of functional groups (e.g., EUDRAGIT® RS-100), and (b) is produced in a batch process from a melt of all ingredients (including active ingredients). See the '999 patent abstract; column 2, lines 32-43;

and column 5, lines 53-67. The '999 patent clearly teaches that a mixture of (meth)acrylate polymers (i) and (ii) is a critical feature of the disclosed therapeutic system. See the'999 patent, also, at column 2, line 47 through column 3, line 23.

In particular, attention is directed to the '999 patent at column 2, lines 50-63:

> By adapting the polymer components such that the resulting polymer combination accepts drugs and other additives such as softeners, penetration-promoting substances, and the like, it is now possible to control the release of drug to the skin and to achieve therapy-specific release profiles.
> The polymer components to be mixed are selected according to the following two important factors:
>
> 1. The influence on drug release through (meth)acrylic polymers containing functional groups.
>
> 2. The influence on the melt and flow behavior of the product blend by poly(meth)acrylates which contain no or only insignificant amounts of functional groups.

Examples of (meth)acrylate copolymers having functional groups are set forth at column 4, lines 1-17 of the '999 patent. These copolymers contain tertiary amino groups, quaternary ammonium groups, or carboxylic acid groups. Nonfunctional (meth)acrylate copolymers, disclosed at column 4, lines 18-36 of the '999 patent, are free of such functional groups or contain only an insignificant amount of such groups.

Moreover, the '999 patent is directed to a specific mixture of copolymers as a matrix mass for the release of an active agent. The system and methods of the '999 patent require a functional and a nonfunctional (meth)acrylate copolymer, and its disclosure provides no motivation for a person skilled in the art to delete either a functional or a nonfunctional (meth)acrylate copolymer from the matrix composition. Indeed, the '999 patent teaches that if one of the (meth)acrylate copolymers is omitted, then either drug release or melt and flow

behavior would be adversely effected. In that way, the '999 patent effectively teaches away from the present invention.

The presently claimed invention differs significantly from that disclosed in the '999 patent. In particular, the present claims recite a matrix composition containing only a EUDRAGIT® RS-100 or an equivalent thereof. See Examples 1-3 of the specification. The present claims recite a matrix composition having a sole, specifically claimed (meth)acrylate copolymer and exclude other (meth)acrylate copolymers.

The '999 patent fails to teach or suggest the presently claimed matrix composition containing a sole meth(acrylate) copolymer (i.e., EUDRAGIT® RS-100 and its equivalents). In contrast, the '999 teachings are limited to a mixture or combination of (meth)acrylate copolymers that contain functional groups and that lack functional groups. In fact, the '999 patent disclosure discourages the use of only nonfunctionalized copolymers (e.g., EUDRAGIT® RS-100), and thereby leads those skilled in the art away from the presently claimed invention. In particular, because the '999 patent teaches the criticality of including blend (meth)acrylate copolymers in the matrix composition, the '999 patent provides no motivation for a person skilled in the art to omit a functional (meth)acrylate copolymer with any reasonable expectation of providing a TTS that effectively delivers sex steroids over a long period of time.

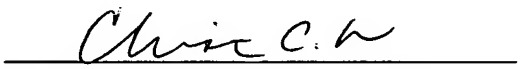
Accordingly, the rejection is properly withdrawn. It is well-known that to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143.

There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the cited references to make the claimed invention, nor is there a reasonable expectation of success.

In view thereof, reconsideration and withdrawal of the §103 rejection are requested.

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,



Christine C. O'Day (Reg. 38,256)
Edwards & Angell, LLP
P.O. Box 9169
Boston, MA 02209
Telephone: 617-439-4444
Fax No.: 617-439-4170